

## SRY gene

sex determining region Y

### Normal Function

The *SRY* gene provides instructions for making a protein called the sex-determining region Y protein. This protein is involved in male-typical sex development, which usually follows a certain pattern based on an individual's chromosomes. People usually have 46 chromosomes in each cell. Two of the 46 chromosomes, known as X and Y, are called sex chromosomes because they help determine whether a person will develop male or female sex characteristics. Girls and women typically have two X chromosomes (46,XX karyotype), while boys and men typically have one X chromosome and one Y chromosome (46,XY karyotype).

The *SRY* gene is found on the Y chromosome. The sex-determining region Y protein produced from this gene acts as a transcription factor, which means it attaches (binds) to specific regions of DNA and helps control the activity of particular genes. This protein starts processes that cause a fetus to develop male gonads (testes) and prevent the development of female reproductive structures (uterus and fallopian tubes).

### Health Conditions Related to Genetic Changes

#### Swyer syndrome

Variants (also called mutations) in the *SRY* gene have been identified in approximately 15 percent of individuals with Swyer syndrome, also known as 46,XY complete gonadal dysgenesis or 46,XY pure gonadal dysgenesis. Swyer syndrome is a condition that affects sex development. Individual with this condition have a male-typical chromosome pattern (46,XY karyotype), but they develop female-typical sex characteristics.

*SRY* gene variants that cause Swyer syndrome prevent production of the sex-determining region Y protein or result in the production of a nonfunctioning protein. Without functional sex-determining region Y protein, a fetus will not develop testes but will develop a uterus and fallopian tubes, despite having an X and a Y chromosome.

#### 46,XX testicular difference of sex development

Changes affecting the *SRY* gene have been found to cause 46,XX testicular difference of sex development. Individuals with this condition have a female-typical chromosome

pattern (46,XX karyotype) but develop male sex characteristics, including testes, though they may be small and undescended.

In most individuals with 46,XX testicular difference of sex development, the condition results from an abnormal exchange of genetic material (translocation) between the Y chromosome and another chromosome, most often the X chromosome. This exchange occurs as a random event during the formation of sperm cells in the affected person's father. In this condition, the *SRY* gene (which is on the Y chromosome) is misplaced, almost always onto an X chromosome. A fetus with an X chromosome that carries the *SRY* gene will develop male sex characteristics despite not having a Y chromosome.

### Other disorders

*SRY* gene variants that impair the function of the sex-determining region Y protein have been identified in a small number of people with 46,XY difference of sex development, or partial gonadal dysgenesis. The effects of these variants on the function of the sex-determining region Y protein is likely less severe than those of variants that cause Swyer syndrome (described above). Individuals with 46,XY difference of sex development have a male-typical chromosome pattern (46,XY karyotype), but they have external genitalia that do not look clearly male or clearly female (ambiguous genitalia) or other abnormalities of the genitals and reproductive organs.

Translocations that misplaced the *SRY* gene onto an X chromosome cause about 10 percent of cases of a condition called ovotesticular difference of sex development. Individuals with this condition have a female-typical chromosome pattern (46,XX karyotype) and tissue from both female and male reproductive organs (ovarian and testicular tissue).

### **Other Names for This Gene**

- essential protein for sex determination in human males
- sex determining region protein
- sex-determining region on Y
- SRY\_HUMAN
- TDF
- TDY
- testis-determining factor

### **Additional Information & Resources**

#### Tests Listed in the Genetic Testing Registry

- Tests of *SRY* ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=6736\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=6736[geneid]))

## Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%28SRY%5BTI%5D%29+OR+%28sex+determining+region+Y%5BTI%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D>)

## Catalog of Genes and Diseases from OMIM

- SEX-DETERMINING REGION Y (<https://omim.org/entry/480000>)

## Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/6736>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=SRY\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=SRY[gene]))

## **References**

- Assumpcao JG, Benedetti CE, Maciel-Guerra AT, Guerra G Jr, Baptista MT, Scolfaro MR, de Mello MP. Novel mutations affecting SRY DNA-binding activity: the HMG box N65H associated with 46,XY pure gonadal dysgenesis and the familial non-HMG box R30I associated with variable phenotypes. *J Mol Med (Berl)*. 2002 Dec;80(12):782-90. doi: 10.1007/s00109-002-0376-9. Epub 2002 Oct 1. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/12483463>)
- Delot EC, Vilain EJ. Nonsyndromic 46,XX Testicular Disorders/Differences of Sex Development. 2003 Oct 30 [updated 2022 May 26]. In: Adam MP, Everman DB, Mirzaa GM, Pagon RA, Wallace SE, Bean LJH, Gripp KW, Amemiya A, editors. GeneReviews(R) [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2023. Available from <http://www.ncbi.nlm.nih.gov/books/NBK1416/> Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/20301589>)
- Gimelli G, Gimelli S, Dimasi N, Bocciardi R, Di Battista E, Prampano T, Zuffardi O. Identification and molecular modelling of a novel familial mutation in the SRY gene implicated in the pure gonadal dysgenesis. *Eur J Hum Genet*. 2007 Jan;15(1):76-80. doi: 10.1038/sj.ejhg.5201719. Epub 2006 Oct 25. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/17063144>)
- Kellermayer R, Halvax L, Czako M, Shahid M, Dhillon VS, Husain SA, Sule N, Gomori E, Mammel M, Kosztolanyi G. A novel frame shift mutation in the HMG box of the SRY gene in a patient with complete 46,XY pure gonadal dysgenesis. *Diagn Mol Pathol*. 2005 Sep;14(3):159-63. doi: 10.1097/01.pas.0000176770.56541.dd. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/16106197>)
- King TF, Conway GS. Swyer syndrome. *Curr Opin Endocrinol Diabetes Obes*. 2014 Dec;21(6):504-10. doi: 10.1097/MED.0000000000000113. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/25314337>)
- Phillips NB, Jancso-Radek A, Ittah V, Singh R, Chan G, Haas E, Weiss MA.

SRYand human sex determination: the basic tail of the HMG box functions as a kineticclamp to augment DNA bending. *J Mol Biol.* 2006 Apr 21;358(1):172-92. doi:10.1016/j.jmb.2006.01.060. Epub 2006 Feb 6. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/v/16504207>)

- Queralt R, Madrigal I, Vallecillos MA, Morales C, Ballesca JL, Oliva R, SolerA, Sanchez A, Margarit E. Atypical XX male with the SRY gene located at the longarm of chromosome 1 and a 1qter microdeletion. *Am J Med Genet A.* 2008 May 15;146A(10):1335-40. doi: 10.1002/ajmg.a.32284. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/18412126>)
- Racca JD, Chen YS, Maloy JD, Wickramasinghe N, Phillips NB, Weiss MA. Structure-function relationships in human testis-determining factor SRY: an aromatic buttress underlies the specific DNA-bending surface of a high mobilitygroup (HMG) box. *J Biol Chem.* 2014 Nov 21;289(47):32410-29. doi:10.1074/jbc.M114.597526. Epub 2014 Sep 24. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/25258310>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4239596/>)
- Rizvi AA. 46, XX man with SRY gene translocation: cytogenetic characteristics, clinical features and management. *Am J Med Sci.* 2008 Apr;335(4):307-9. doi:10.1097/MAJ.0b013e31811ec1b4. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/v/18414071>)
- Shahid M, Dhillon VS, Jain N, Hedau S, Diwakar S, Sachdeva P, Batra S, DasBC, Husain SA. Two new novel point mutations localized upstream and downstream ofthe HMG box region of the SRY gene in three Indian 46,XY females with sexreversal and gonadal tumour formation. *Mol Hum Reprod.* 2004 Jul;10(7):521-6. doi:10.1093/molehr/gah071. Epub 2004 May 21. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/15155818>)
- Sreenivasan R, Gonen N, Sinclair A. SOX Genes and Their Role in Disorders of Sex Development. *Sex Dev.* 2022;16(2-3):80-91. doi: 10.1159/000524453. Epub 2022Jun 27. Citation on PubMed (<https://www.ncbi.nlm.nih.gov/pubmed/35760052>)
- Waters PD, Wallis MC, Marshall Graves JA. Mammalian sex--Origin and evolutionof the Y chromosome and SRY. *Semin Cell Dev Biol.* 2007 Jun;18(3):389-400. doi:10.1016/j.semcdb.2007.02.007. Epub 2007 Feb 24. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/17400006>)

## Genomic Location

The SRY gene is found on the Y chromosome (<https://medlineplus.gov/genetics/chromosome/y/>).

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